

USSN 10/607,922
Pandey
Preliminary Amendment

IN THE SPECIFICATION:

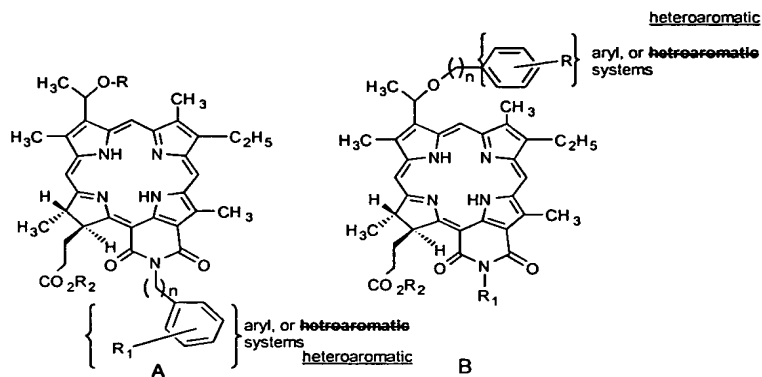
Please amend the specification as follows:

Please amend the paragraph on page 2, lines 4-22, of the Specification as follows:

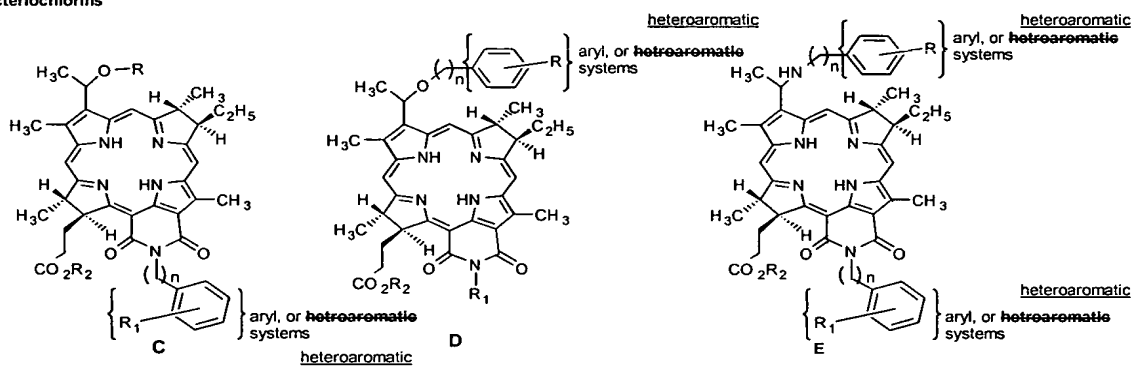
In photodynamic therapy, a photosensitizer compound that demonstrates the ability to selectively accumulate in target tissue, such as neoplastic or hyperproliferative tissue, is administered to a subject, and when the photosensitizer accumulates in or preferentially associates with the target tissue, the target tissue becomes sensitized to photoradiation. The photo-sensitizing agent can be activated by either coherent (laser) or non-coherent (non-laser) light. It is currently accepted that following absorption of light, the photosensitizer is transformed from its ground singlet state (P) into an electronically excited triplet state ($^3P^*$; $\tau \sim 10^{-2}$ sec.) via a short-lived excited singlet state ($^1P^*$; $\tau \sim 10^{-6}$ sec.) The excited triplet can undergo non-radiative decay or participate in an electron transfer process with biological substrates to form radicals and radical ions, which can produce singlet oxygen and superoxide (O_2^-) after interaction with molecular oxygen (O_2). Singlet oxygen can be produced from molecular oxygen by the transfer of energy directly or indirectly from the activated photosensitizer. Singlet oxygen is one of the agents responsible for cellular and tissue damage in PDT, causing oxidation of the target tissue; there also is evidence that the superoxide ion may be involved. The generation of these cytotoxic agents plays a role in tumor homeostasis and the observed tumor destruction.

Please amend the structures on page 10, lines 1-17, of the Specification as follows:

Chlorins:



Bacteriochlorins



Where R and R_1 = Various alkyl with variable no. of carbon chains
their fluorinated analogs, aromatic side chain with fluorinated or
non-fluorinated substituents.

R_2 = Fluorinated or non-fluorinated ester groups with variable no. of carbon units,
Fluorinated and non-fluorinated amide substituents

USSN 10/607,922

Pandey

Preliminary Amendment

Please amend the paragraph on page 23, lines 23-32, of the Specification as follows:

As used herein, sample refers to anything that contains ~~[[an]]~~ a target for which a target assay is desired. The sample can be a biological sample, such as a biological fluid or a biological tissue. Examples of biological fluids include urine, blood, plasma, serum, saliva, semen, stool, sputum, cerebral spinal fluid, tears, mucus, sperm, amniotic fluid or the like. Biological tissues are aggregates of cells, usually of a particular kind together with their intercellular substance that form one of the structural materials of a human, animal, plant, bacterial, fungal or viral structure, including connective, epithelium, muscle and nerve tissues. Examples of biological tissues also include organs, tumors, lymph nodes, arteries and individual cell(s).

Please amend the paragraph on page 60, line 20 through page 61, line 2, of the Specification as follows:

Many compounds that can serve as targets for ligand-receptor binding pairs, and more specifically, antibodies, have been identified, and the techniques to construct conjugates of such ligands with photosensitizers are well known to those of ordinary skill in this art. For example, Rakestraw *et al.* teaches conjugating Sn(IV) chlorin e via covalent bonds to monoclonal antibodies using a modified dextran carrier (Rakestraw, S. L., Tompkins, R. D., and Yarmush, M. L., *Proc. ~~[[Nad]]~~ Natl. Acad. Sci. USA* 87: 4217-4221 (1990)). The compounds disclosed herein can also be conjugated to a ligand, such as an antibody, by using a coupling agent. Any bond which is capable of linking the components such that they are stable under physiological conditions for the time needed for administration and treatment is suitable, but covalent linkages are preferred. The link between two components may be direct, *e.g.*, where a photosensitizer is linked directly to a targeting agent, or indirect, *e.g.*, where a photosensitizer is linked to an intermediate and that intermediate being linked to the targeting agent.

Please amend the paragraph on page 88, lines 16-24, of the Specification as follows:

USSN 10/607,922

Pandey

Preliminary Amendment

[[An]] A target compound provided herein is formulated to bind with great affinity to *Mycobacterium tuberculosis* in a selective and specific manner. Preferably, the targeted compound is formulated as an aerosol, which can be easily inhaled, enabling distribution into all lung segments. Steam is then inhaled to solubilize any unbound targeted compound and facilitate its removal from the lung by exhalation. Alternatively, the targeted compound is formulated as an injectable compound and administered intravenously. Either way, the bound targeted compound is photoactivated by an external light source disposed on the chest and/or back.

REMARKS

Any fees that may be due in connection with filing this paper, or during the entire pendency of this application, may be charged to Deposit Account No. 50-1213.

The Specification is amended to correct obvious typographical and formatting errors. The amendment to the paragraph on page 2, line 9, of the specification adds the inadvertently omitted preposition "by" after the word "activated" for grammatical clarity. The amendment to the structures on page 10, lines 1-17, of the Specification replaces the word "hetroaromatic" with "heteroaromatic" for clarity. The amendment to the paragraphs on page 23, lines 23-32 and page 88, lines 16-24, of the Specification replaces the article "an" with "a" for grammatical clarity. The amendment to the paragraph on page 60, line 20 through page 61 line 2, of the specification replaces "Nad" with "NatI" for proper abbreviation of the referenced citation. No new matter has been added.

Applicant notes that replacement formal drawings containing Figures 3,4,9 and 10 were submitted on August 6, 2003 under a separate cover. No new matter has been added.

* * *

USSN 10/607,922
Pandey
Preliminary Amendment

Entry of this amendment and examination of this application are respectfully requested.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By: 
Dale L. Rieger
Registration No. 43,045

Attorney Docket No.: 25886-0094
Address all correspondence to:
Stephanie L. Seidman, Esq.
HELLER EHRMAN WHITE & McAULIFFE LLP
4350 La Jolla Village Drive, 7th Floor
San Diego, California 92122-1246
Telephone: (858) 450-8400
Facsimile: (858) 587-5360
EMAIL: sseidman@hewm.com